Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (currently amended) A tissue-adhesive formulation comprising ~~consisting of~~ a naturally occurring or synthetic polymerisable and/or cross-linkable material in particulate form, the polymerisable and/or cross-linkable material being in admixture with particulate material comprising tissue-reactive functional groups.

2. (original) A formulation according to Claim 1, wherein the ratio of polymerisable and/or cross-linkable material to material comprising tissue-reactive functional groups is between 0.1:1 and 10:1.

3. (original) A formulation according to Claim 2, wherein the ratio of polymerisable and/or cross-linkable material to material comprising tissue-reactive functional groups is between 0.2:1 and 1:1.

4. (currently amended) A formulation according to ~~any preceding claim~~ Claim 1, wherein the tissue-reactive functional groups are selected from the group consisting of imido ester, p- nitrophenyl carbonate, N-hydroxysuccinimide ester, epoxide, isocyanate, acrylate, vinyl sulfone, orthopyridyl-disulfide, maleimide, aldehyde and iodoacetamide.

5. (original) A formulation according to Claim 4, wherein the tissue-reactive functional groups are N-hydroxysuccinimide esters.

6. (currently amended) A formulation according to ~~any preceding claim~~ Claim 1, wherein the formulation contains one type of material comprising tissue-reactive functional groups.

7. (currently amended) A formulation according to ~~any one of Claims 1 to 5~~ Claim 1, wherein the formulation contains two types of ~~materials~~ material comprising tissue-reactive functional groups.

8. (currently amended) A formulation according to ~~any preceding claim~~ Claim 1, wherein the material comprising tissue-reactive functional groups is formed by derivatization of a polymer precursor.

9. (original) A formulation according to Claim 8, wherein all or substantially all of the available sites in the polymer precursor are derivatised.

10. (currently amended) A formulation according to Claim 8 ~~or Claim 9~~, wherein the polymer precursor contains carboxylic acid or alcohol functional groups.

11. (original) A formulation according to Claim 10, wherein the polymer precursor is selected from the group consisting of sucrose, cellulose and polyvinylalcohol.

12. (original) A formulation according to Claim 10, wherein the polymer precursor is formed by polymerisation of two or more monomers, and at least one of the monomers contains a carboxylic acid group or a group capable of being reacted with another material to form an acid functionality.

13. (original) A formulation according to Claim 12, wherein the monomers are selected from the group consisting of *N*-vinyl-2-pyrrolidone, acrylic acid, vinyl acetate, vinyl acetic acid, mono-2-(methacryloyloxy) ethyl succinate, methacrylic acid, 2-hydroxyethyl methacrylate, 2-hydroxypropyl methacrylate and (polyethylene glycol) methacrylate.

14. (currently amended) A formulation according to Claim 12 ~~or Claim 13~~, wherein polymerisation is initiated by a free radical initiator.

15. (original) A formulation according to Claim 14, wherein the initiator is selected from the group consisting of benzoyl peroxide, 2,2'-azobisisobutyronitrile, lauroyl peroxide and peracetic acid.

16. (currently amended) A formulation according to ~~any one of Claims 12 to 15~~ Claim 13, wherein the polymer precursor is poly (N-vinyl-2-pyrrolidone-co-acrylic acid) co-polymer.

17. (currently amended) A formulation according to Claim 16, wherein the poly (N-vinyl-2-pyrrolidone-co-acrylic acid) co-polymer has a molar ratio of acrylic acid-derived units less than 0.60 ~~0. 60, more preferably less than 0.40~~.

18. (original) A formulation according to Claim 16, wherein the poly (N-vinyl-2-pyrrolidone-co-acrylic acid) co-polymer has a molar ratio of acrylic acid-derived units between 0.025 and 0.25.

19. (currently amended) A formulation according to ~~any one of Claims 7 to 18~~ Claim 8, wherein the polymer precursor is derivatised with N-hydroxysuccinimide to form the material comprising tissue-reactive functional groups.

20. (original) A formulation according to Claim 19, wherein the material comprising tissue-reactive functional groups is an N-hydroxysuccinimide ester of poly(N-vinyl-2-pyrrolidone-co-acrylic acid) co-polymer.

21. (original) A formulation according to Claim 20, wherein the material comprising tissue-reactive functional groups has a molar ratio of acrylic acid-derived units between 0.05 and 0.50 and vinyl pyrrolidone-derived units between 0.50 and 0.95.

22. (currently amended) A formulation according to ~~any preceding claim~~ Claim 1, wherein the concentration of material comprising tissue-reactive functional groups in the formulation is between 10 and 50% w/w.

23. (currently amended) A formulation according to ~~any preceding claim~~ Claim 1, wherein the polymerisable and/or cross-linkable material is selected from the group consisting of polysaccharides, polylactates, polyols and proteins, and derivatives thereof.

24. (currently amended) A formulation according to ~~any one of Claims 1 to 22~~ Claim 1, wherein the polymerisable and/or cross-linkable material ~~is, or further comprises,~~ is a chemically modified polyalkylene glycol containing multiple primary amino or thiol groups.

25. (original) A formulation according to Claim 23, wherein the polymerisable and/or cross-linkable material is cross-linked.

26. (currently amended) A formulation according to Claim 23 ~~or Claim 25~~, wherein the polyymerisable and/or cross-linkable material is albumin.

27. (currently amended) A formulation according to Claim 26, wherein the albumin ~~polymerisable and/or cross-linkable material~~ is porcine, bovine or human albumin.

28. (currently amended) A formulation according to ~~any preceding claim~~ Claim 1, wherein the polymerisable and/or cross-linkable material is buffered to a pH greater than 7.

29. (currently amended) A formulation according to ~~any preceding claim~~ Claim 1, further comprising one or more ~~further~~ components selected from the group of structural polymers, surfactants, plasticisers and ~~other~~ excipients.

30. (currently amended) A formulation according to ~~any preceding claim~~ Claim 1, wherein the particles that make up the formulation have a median size in the range 5μm to 500μm~~, more preferably 5um to 100um~~.

31. (currently amended) A sheet having a multilayer structure, said structure consisting of a core of a naturally occurring or synthetic polymeric material, the core being coated on at least one side thereof with a tissue-adhesive formulation according to ~~any preceding claim~~ Claim 1.

32. (currently amended) A sheet according to Claim 31, wherein the core comprises a polymeric material selected from the group consisting of polymers or co-polymers based on α-hydroxy acids~~such as polylactide, polyglycolide, polycaprolactone and other polylactones such as butyro and valerolactone~~.

33. (original) A sheet according to Claim 31, wherein the core comprises polymeric material selected from the group consisting of alginates, polyhydroxyalkanoates, polyamides, polyethylene, propylene glycol, water-soluble glass fibre, starch, cellulose, collagen, pericardium, albumin, polyester, polyurethane, potyetheretherketone, polypropylene and polytetrafluoroethylene.

34. (currently amended) A sheet according to ~~any one of Claims 30 to 33~~ Claim 31, wherein the core is apertured.

35. (original) A sheet according to Claim 34, wherein the sheet has a regular array of apertures, and the apertures are between 50μm and 2mm in diameter and adjacent apertures are formed at a centre-to-centre separation of between 100μm and 5mm.

36. (original) A sheet according to Claim 35, wherein the apertures account for between 5% and 80% of the overall surface area of the core.

37. (currently amended) A sheet according to ~~any one of Claims 30 to 36~~ Claim 31, wherein the core has a thickness of 0.005 to 5mm.

38. (currently amended) A sheet according to ~~any one of Claims 30 to 37~~ Claim 31, wherein the tissue-adhesive formulation is applied to the core by mechanically compressing a blend of material containing tissue-reactive functional groups and polymerisable and/or cross-linkable material, both in particulate form, onto one or both sides of the core.

39. (currently amended) A sheet according to Claim ~~38~~ 31, wherein the core is coated on both sides with the ~~said blend of material~~ tissue-adhesive formulation.

40. (currently amended) A sheet according to Claim ~~39~~ 31, wherein one surface of the sheet is coated with a non-adhesive material.

41. (original) A sheet according to Claim 40, wherein the non-adhesive material is selected from the group consisting of polyethylene glycols, polylactide and poly(lactide-co-glycolide).

42. (original) A sheet according to Claim 41, wherein the non-adhesive coating includes a visibly-absorbing chromophore.

43. (original) A sheet according to Claim 42, wherein the visibly-absorbing chromophore is methylthioninium chloride.

44. (currently amended) A sheet according to ~~any one of Claims 40 to 43~~ Claim 40, wherein the coating of non-adhesive material is apertured.

45. (original) A biocompatible and hydratable composition suitable for topical application to internal or external surfaces of the body, which composition comprises a polymer containing tissue-reactive functional groups and a polymer containing groups that are not tissue-reactive functional groups but which are capable of forming hydrogen bonds with groups at the surface of a tissue to which the matrix is applied.

46. (original) A composition as claimed in Claim 45, wherein the tissue-reactive functional groups are selected from the group consisting of imido ester, p-nitrophenyl carbonate, N-hydroxysuccinimide ester, epoxide, isocyanate, acrylate, vinyl sulfone, orthopyridyl-disulfide, maleimide, aldehyde and iodoacetamide, and the groups that are capable of forming hydrogen bonds are selected from amide, lactam, carbonyl, carboxyl, hydroxyl and ether groups.

47. (currently amended) A composition as claimed in Claim 45 ~~or Claim 46~~, wherein the tissue-reactive groups and the groups that are capable of forming hydrogen bonds are present in the same polymer.

48. (original) A composition as claimed in Claim 47, wherein the tissue-reactive groups are tissue-reactive ester groups, and the groups that are capable of forming hydrogen bonds are amide or lactam groups.

49. (original) A composition as claimed in Claim 48, wherein the polymer is activated PVP-co-PAA.

50. (original) A composition as claimed in Claim 49, wherein the polymer is NHS-activated PVP-co-PAA.

51. (currently amended) A composition as claimed in ~~any one of Claims 45 to 50~~ Claim 45, which has the form of a sheet, patch, or film ~~or the like~~.

52. (currently amended) A method for the manufacture of a sheet according to Claim 31 ~~any one of Claims 31 to 44~~, which method comprises forming a core consisting of naturally occurring or synthetic polymeric material, and coating at least one side of said core with a tissue-adhesive formulation comprising a blend of a naturally occurring or synthetic polymerisable and/or cross-linkable material in particulate form and particulate material consisting of tissue-reactive functional groups.

53. (currently amended) A method of joining a tissue surface to another tissue, or of sealing a tissue surface, which method comprises applying to the tissue surface a formulation according to ~~any one of Claims 1 to 30, a sheet according to any one of Claims 31 to 44 or a composition according to any one of Claims 45 to 51~~ Claim 1.

54-62. (canceled)

63. (new) A method as claimed in Claim 53, wherein the formulation is present on a sheet having a multilayer structure consisting of a core formed of a naturally occurring or synthetic polymeric material, with the formulation being present as a coating on at least one side of the core.

64. (new) A method as claimed in Claim 53, wherein the method is carried out to enhance wound healing, promote wound closure, provide reinforcement in hernia repair

procedures, seal joint tubular structures, seal resected tissue sections, seal air leaks in lung tissue, promote haemostasis, prevent post-surgical adhesions, or deliver a drug or other therapeutic agent.

65. (new) A method of joining a tissue surface to another tissue, or of sealing a tissue surface, which method comprises applying to the tissue surface a composition according to Claim 45.

66. (new) A method as claimed in Claim 65, wherein the method is carried out to enhance wound healing, promote wound closure, provide reinforcement in hernia repair procedures, seal joint tubular structures, seal resected tissue sections, seal air leaks in lung tissue, promote haemostasis, prevent post-surgical adhesions, or deliver a drug or other therapeutic agent.

67. (new) A formulation according to Claim 1, which consists essentially of said naturally occurring or synthetic polymerisable and/or cross-linkable material in particulate form and said particulate material comprising tissue-reactive groups.